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(FILE 'HOME' ENTERED AT 14:36:47 ON 17 NOV 2000)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:37:01 ON 17 NOV 2000

L1 1450 S WHEY(W)ACID?(W)PROTEIN OR WAP
L2 378 S L1(6A)(PROMOTER OR PROMOTOR OR REGULATORY(W)SEQUENCE OR ENHAN
L3 117917 S EXPRESS?(10A)(HUMAN(5A)CELL)
L4 5 S L2 AND L3
L5 3 DUP REM L4 (2 DUPLICATES REMOVED)

=> d bib ab 1-3 l5

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1999:95239 CAPLUS
DN 130:277412
TI In vivo and in vitro expression of human serum albumin genomic sequences in mammary epithelial cells with .beta.-lactoglobulin and **whey acidic protein promoters**
AU Barash, Itamar; Faerman, Alexander; Richenstein, Moshe; Kari, Rachel; Damary, Golda-Meir; Shani, Moshe; Bissell, Mina J.
CS Institute of Animal Science, The Volcani Center, Agricultural Research Organization, Bet Dagan, 50250, Israel
SO Mol. Reprod. Dev. (1999), 52(3), 241-252
CODEN: MREDEE; ISSN: 1040-452X
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The expression pattern of human serum albumin (HSA) in transgenic mice carrying various HSA genomic sequences driven either by the mouse whey acidic protein (**WAP**) or the sheep .beta.-lactoglobulin (BLG) **promoters**, was compared. The pattern of HSA expression in both WAP/HSA and BLG/HSA transgenic lines was copy no. independent, and the major site of ectopic expression was the skeletal muscle. Although an equal proportion of expressors was detd. in both sets of mice (.apprx.25% secreting >0.1 mg/mL), the highest level of HSA secreted into the milk in the WAP/HSA transgenic lines was one order of magnitude lower than in the BLG/HSA lines. Despite this difference, the HSA expression patterns in the mammary gland were similar and consisted of two levels of variegated expression. Studies using mammary explant cultures revealed a comparable responsiveness to the lactogenic hormones insulin, hydrocortisone, and prolactin, although the WAP/HSA gene constructs were more sensitive to the hydrocortisone effect than were the BLG/HSA vectors. When HSA vectors were stably transfected into the mouse mammary cell line CID-9, they displayed a hierarchy of expression, dependent upon the specific complement of HSA introns included. Nevertheless, the expression of HSA in four out of five WAP/HSA constructs was similar to their BLG/HSA counterparts. This construct-dependent, and promoter-independent, hierarchy was also found following transfection into the newly established Golda-1 ovine mammary epithelial cell line.
RE.CNT 57
RE

(1) Ali, S; Mol Cell Biol 1988, V199, P415 CAPLUS
(2) Archibald, A; Proc Natl Acad Sci USA 1990, V87, P5178 CAPLUS
(3) Auffray, C; Eur J Biochem 1980, V107, P303 CAPLUS
(4) Barash, I; Anim Biotech 1993, V4, P203 CAPLUS
(5) Barash, I; Mol Cell Biochem 1995, V144, P175 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1997:265594 CAPLUS
DN 126:247559
TI Rodent whey acid protein (**WAP**) or mouse mammary tumor virus (MMTV) **regulatory sequences** for targeted **expression** of heterologous genes in **human** mammary **cells** and applications in carcinoma gene therapy
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
PA Bavarian Nordic Research Institute A/s, Den.; Gsf - Forschungszentrum Fuer Umwelt Und Gesundheit; Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9709440	A1	19970313	WO 1996-EP3922	19960906
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
	AU 9669876	A1	19970327	AU 1996-69876	19960906
	EP 848757	A1	19980624	EP 1996-931040	19960906
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11511979	T2	19991019	JP 1996-510876	19960906
PRAI	DK 1995-976	19950906			
	WO 1996-EP3922	19960906			

AB The present invention relates to the use of the **WAP** or MMTV **regulatory sequences** for the targeted **expression** of linked heterologous DNA sequences in **human** mammary **cells**, including **human** mammary carcinoma **cells**. Viral or plasmid vectors are constructed for heterologous gene expression, esp. for expression of therapeutic genes.

L5 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
AN 95358828 MEDLINE
DN 95358828
TI The effect of various introns and transcription terminators on the efficiency of expression vectors in various cultured cell lines and in the mammary gland of transgenic mice.
AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G; Stinnakre M G; Pointu H; Puissant C; Houdebine L M
CS Agriculture et Agro-Alimentaire Canada, Est Lennoxville, Quebec.
SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.
Journal code: AL6. ISSN: 0168-1656.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 199511

AB Various combinations of promoters, introns and transcription terminators were used to drive the **expression** of bovine growth hormone (bGH) cDNA in different **cell** types. In constructs containing the **human** cytomegalovirus (hCMV) promoter and the SV40 late genes terminator, the intron from SV40 genes (VP1) was much more efficient, than the intron from the early genes (t). The synthetic intron SIS generated by the association of an adenovirus splice donor and an immunoglobulin G splice acceptor showed the highest activity. The respective potency of these introns was similar in several mammalian (CHO, HC11 and COS) and fish (TO2 and EPC) cells. The rabbit **whey acidic protein** (**WAP**) gene **promoter** was highly efficient to drive the expression of bGH gene in the HC11 mammary cell lines. In contrast, the bGH cDNA under the control of the same promoter was much less efficiently expressed when the SV40 VP1 intron and transcription terminator were used. The rabbit WAP gene and the human GH gene terminators did not or only moderately enhanced the expression of the construct **WAP** bGH cDNA. Introduction of a **promoter** sequence from the mouse mammary tumor virus (MMTV) LTR in the VP1 intron increased very significantly the expression of the WAP bGH cDNA. Although several of these vectors showed high potency when expressed stably in HC11 cells, all of them were only moderately efficient in transgenic mice. These data indicate that the VP1 and the SIS introns may be used to express foreign cDNAs with good efficiency in different cell types. The addition of an enhancer within an intron may still reinforce its efficiency. However, transfection experiments, even when stable expression is carried out, are poorly predictive of the potential efficiency of a vector in transgenic animals.

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(FILE 'HOME' ENTERED AT 16:21:12 ON 14 NOV 2000)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:21:27 ON 14 NOV 2000

L1 10027 S (MURINE OR MOUSE)(W)MAMMARY(W)TUMOR(W)VIRUS OR MMTV
L2 2247 S L1(6A)(PROMOTER OR PROMOTOR OR REGULATORY(W)SEQUENCE OR ENHAN
L3 117802 S EXPRESS?(10A)(HUMAN(5A)CELL)
L4 100 S L2 AND L3
L5 47 DUP REM L4 (53 DUPLICATES REMOVED)

=> d 1-47 au ti so l5

L5 ANSWER 1 OF 47 MEDLINE DUPLICATE 1
AU Kinyamu H K; Fryer C J; Horwitz K B; Archer T K
TI The **mouse mammary tumor virus** **promoter** adopts distinct chromatin structures in human breast cancer cells with and without glucocorticoid receptor.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 30) 275 (26) 20061-8.
Journal code: HIV. ISSN: 0021-9258.

L5 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Brandt, Ralf; Eisenbrandt, Ralf; Leenders, Frauke; Zschiesche, Wolfgang; Binas, Bert; Juergensen, Carola; Theuring, Franz
TI Mammary gland specific hEGF receptor transgene expression induces neoplasia and inhibits differentiation
SO Oncogene (2000), 19(17), 2129-2137
CODEN: ONCNES; ISSN: 0950-9232

L5 ANSWER 3 OF 47 MEDLINE DUPLICATE 2
AU Neyns B; Teugels E; Bourgain C; Birrerand M; De Gr`eve J
TI Alteration of jun proto-oncogene status by plasmid transfection affects growth of human ovarian cancer cells.
SO INTERNATIONAL JOURNAL OF CANCER, (1999 Aug 27) 82 (5) 687-93.
Journal code: GQU. ISSN: 0020-7136.

L5 ANSWER 4 OF 47 MEDLINE DUPLICATE 3
AU Bouhon I A; Shinkai M; Honda H; Mizuno M; Wakabayashi T; Yoshida J; Kobayashi T
TI Synergism between mild hyperthermia and interferon-beta gene expression.
SO CANCER LETTERS, (1999 May 24) 139 (2) 153-8.
Journal code: CMX. ISSN: 0304-3835.

L5 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Asselbergs, Fred A. M.; Grossenbacher, Rita; Ortmann, Rainer; Hengerer, Bastian; Mcmaster, Gary K.; Sutter, Esther; Widmer, Roland; Buxton, Frank
TI Position-independent expression of a human nerve growth factor-luciferase reporter gene cloned on a yeast artificial chromosome vector
SO Nucleic Acids Res. (1998), 26(7), 1826-1833
CODEN: NARHAD; ISSN: 0305-1048

L5 ANSWER 6 OF 47 MEDLINE DUPLICATE 4
AU Desarnaud F; Do Thi A N; Brown A M; Lemke G; Suter U; Baulieu E E; Schumacher M

TI Progesterone stimulates the activity of the promoters of peripheral myelin protein-22 and protein zero genes in Schwann cell
SO JOURNAL OF NEUROCHEMISTRY, (1998 Oct) 71 (4) 1765-6.
Journal code: JAV. ISSN: 0022-3042.

L5 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5
AU Myal, Yvonne; Iwasiow, Barbara; Cosby, Helle; Yarmill, Alison; Shiu, Robert P. C.
TI Mouse mammary tumor virus (MMTV)-targeted gene expression of the human gross cystic disease fluid protein-15/prolactin inducible protein (GCDFP-15/PIP) in the mammary gland of transgenic mice
SO Transgenics (1998), 2(3), 327-332
CODEN: TADTEF; ISSN: 1023-6171

L5 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Schoonen, W. G. E. J.; Dijkema, R.; De Ries, R. J. H.; Wagenaars, J. L.; Joosten, J. W. H.; De Gooyer, M. E.; Deckers, G. H.; Kloosterboer, H. J.
TI Human progesterone receptor A and B isoforms in CHO cells. II. Comparison of binding, transactivation and ED50 values of several synthetic (anti)progestagens in vitro in CHO and MCF-7 cells and in vivo in rabbits and rats
SO J. Steroid Biochem. Mol. Biol. (1998), 64(3-4), 157-170
CODEN: JSBBEZ; ISSN: 0960-0760

L5 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
TI Rodent whey acid protein (WAP) or **mouse mammary tumor virus** (**MMTV**) **regulatory sequences** for targeted **expression** of heterologous genes in **human** mammary **cells** and applications in carcinoma gene therapy
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

L5 ANSWER 10 OF 47 MEDLINE DUPLICATE 6
AU Asano T; Zwelling L A; An T; McWatters A; Herzog C E; Mayes J; Loughlin S M; Kleinerman E S
TI Effect of transfection of a Drosophila topoisomerase II gene into a human brain tumour cell line intrinsically resistant to etoposide.
SO BRITISH JOURNAL OF CANCER, (1996 Jun) 73 (11) 1373-80.
Journal code: AV4. ISSN: 0007-0920.

L5 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU McIlhinney, R. A. J.; Molnar, E.; Atack, J. R.; Whiting, P. J.
TI **Cell** surface **expression** of the **human** N-methyl-D-aspartate receptor subunit 1a requires the co-**expression** of the NR2A subunit in transfected cells
SO Neuroscience (Oxford) (1996), 70(4), 989-97
CODEN: NRSCDN; ISSN: 0306-4522

L5 ANSWER 12 OF 47 MEDLINE DUPLICATE 7
AU Archer T K; Fryer C J; Lee H L; Zaniewski E; Liang T; Mymryk J S
TI Steroid hormone receptor status defines the **MMTV** **promoter** chromatin structure in vivo.
SO JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (1995 Jun) 53 (1-6) 421-9. Ref: 54
Journal code: AX4. ISSN: 0960-0760.

L5 ANSWER 13 OF 47 MEDLINE DUPLICATE 8
AU Xu A; Kudo S; Fukuda M
TI A novel expression vector composed of a regulatory element of the human leukosialin-encoding gene in different types of mammalian cells.
SO GENE, (1995 Jul 28) 160 (2) 283-6.

Journal code: FOP. ISSN: 0378-1119.

L5 ANSWER 14 OF 47 MEDLINE DUPLICATE 9
AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Boffraud P; Kann G; Stinnakre M G; Pointu H; Puissant C; Houdebine L M
TI The effect of various introns and transcription terminators on the efficiency of expression vectors in various cultured cell lines and in the mammary gland of transgenic mice.
SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.
Journal code: AL6. ISSN: 0168-1656.

L5 ANSWER 15 OF 47 MEDLINE DUPLICATE 10
AU Wilson S E; Weng J; Blair S; He Y G; Lloyd S
TI Expression of E6/E7 or SV40 large T antigen-coding oncogenes in human corneal endothelial cells indicates regulated high-proliferative capacity.
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1995 Jan) 36 (1) 32-40.

Journal code: GWI. ISSN: 0146-0404.

L5 ANSWER 16 OF 47 MEDLINE DUPLICATE 11
AU Berard J; Gaboury L; Landers M; De Repentigny Y; Houle B; Kothary R; Bradley W E
TI Hyperplasia and tumours in lung, breast and other tissues in mice carrying a RAR beta 4-like transgene.
SO EMBO JOURNAL, (1994 Dec 1) 13 (23) 5570-80.
Journal code: EMB. ISSN: 0261-4189.

L5 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
AU Pendse, Girish J.; Bailey, James E.
TI Effect of Vitreoscilla hemoglobin expression on growth and specific tissue plasminogen activator productivity in recombinant Chinese hamster ovary cells
SO Biotechnol. Bioeng. (1994), 44(11), 1367-70
CODEN: BIBIAU; ISSN: 0006-3592

L5 ANSWER 18 OF 47 MEDLINE DUPLICATE 13
AU Archer T K; Zaniewski E; Moyer M L; Nordeen S K
TI The differential capacity of glucocorticoids and progestins to alter chromatin structure and induce gene **expression** in **human** breast cancer **cells**.
SO MOLECULAR ENDOCRINOLOGY, (1994 Sep) 8 (9) 1154-62.
Journal code: NGZ. ISSN: 0888-8809.

L5 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Thomsen, J. S.; Wang, X.; Hines, R. N.; Safe, S. H.
TI Restoration of Ah-responsiveness in MDA-MB-231 human breast cancer cells by the estrogen receptor
SO Organohalogen Compd. (1993), 13(Dioxin '93, 13th International Symposium on Chlorinated Dioxins and Related Compounds, 1993), 265-8
CODEN: ORCOEP

L5 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Stoecklin, Elisabeth; Botteri, Florence; Groner, Bernd
TI An activated allele of the c-erbB-2 oncogene impairs kidney and lung function and causes early death of transgenic mice
SO J. Cell Biol. (1993), 122(1), 199-208
CODEN: JCLBA3; ISSN: 0021-9525

L5 ANSWER 21 OF 47 MEDLINE DUPLICATE 14
AU Legrand C; Rommelaere J; Caillet-Fauquet P
TI MVM(p) NS-2 protein **expression** is required with NS-1 for maximal

cytotoxicity in **human** transformed **cells**.
SO VIROLOGY, (1993 Jul) 195 (1) 149-55.
Journal code: XE[redacted] ISSN: 0042-6822.

L5 ANSWER 22 OF 47 MEDLINE DUPLICATE 15
AU Haraguchi S; Good R A; Engelman R W; Day N K
TI Human prolactin regulates transfected MMTV LTR-directed gene **expression** in a **human** breast-carcinoma **cell** line through synergistic interaction with steroid hormones.
SO INTERNATIONAL JOURNAL OF CANCER, (1992 Dec 2) 52 (6) 928-33.
Journal code: GQU. ISSN: 0020-7136.

L5 ANSWER 23 OF 47 MEDLINE DUPLICATE 16
AU Momozaki N; Oh-Uchida M; Tabuchi K; Ikezaki K; Hori K
TI Suppression of anchorage-independent growth of human glioblastoma cell by major histocompatibility complex class I gene-transfection.
SO JOURNAL OF NEUROSURGERY, (1992 May) 76 (5) 845-9.
Journal code: JD3. ISSN: 0022-3085.

L5 ANSWER 24 OF 47 MEDLINE DUPLICATE 17
AU Huper G; Marks J R; Wiener J R; Iglehart J D
TI Relative promoter activity in **human** mammary epithelial **cells** assayed by transient **expression**.
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY, (1992 Nov-Dec) 28A (11-12) 730-4.
Journal code: HEQ. ISSN: 0883-8364.

L5 ANSWER 25 OF 47 MEDLINE DUPLICATE 18
AU Shay J W; West M D; Wright W E
TI Re-expression of senescent markers in deinduced reversibly immortalized cells.
SO EXPERIMENTAL GERONTOLOGY, (1992 Sep-Dec) 27 (5-6) 477-92.
Journal code: EPQ. ISSN: 0531-5565.

L5 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Ricketts, Michael H.; Chiao, Eric; Hu, Meng Chun; Chung, Bon Chu
TI Amplification of P450c21 expression in cultured mammalian cells
SO Biochem. Biophys. Res. Commun. (1992), 186(1), 426-31
CODEN: BBRCA9; ISSN: 0006-291X

L5 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Wang, Qingping; Maher, Veronica M.; McCormick, J. Justin
TI Mammalian expression vectors with modulatable promoters and two multiple cloning sites
SO Gene (1992), 119(2), 155-61
CODEN: GENED6; ISSN: 0378-1119

L5 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Valle, Francesco D.; Callegaro, Lanfranco; Negro, Alessandro
TI Expression vector for the manufacture of nerve growth factor .beta.-subunit in animal cell culture
SO Can. Pat. Appl., 39 pp.
CODEN: CPXXEB

L5 ANSWER 29 OF 47 MEDLINE DUPLICATE 19
AU De Benedetti A; Rhoads R E
TI A novel BK virus-based episomal vector for expression of foreign genes in mammalian cells.
SO NUCLEIC ACIDS RESEARCH, (1991 Apr 25) 19 (8) 1925-31.
Journal code: O8L. ISSN: 0305-1048.

L5 ANSWER 30 OF 47 SCISEARCH COPYRIGHT 2000 ISI (R)
AU DEBENEDETTI A; RHOADS R E (Reprint)
TI A NOVEL BK VIRUS-BASED EPISOMAL VECTOR FOR EXPRESSION OF FOREIGN GENES IN MAMMALIAN-CELLS

SO NUCLEIC ACIDS RESEARCH, (1991) Vol. 19, No. 8, pp. 1925-1931.

L5 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Momozaki, Nobuaki; Tabuchi, Kazuo; Ohuchida, Mamoru; Ikezaki, Kiyonobu; Hirotsu, Tatsumi; Hori, Katsuji
TI The influence of MHC class I expression on the growth of a glioblastoma cell line
SO Biol. Aspects Brain Tumors, Proc. Nikko Brain Tumor Conf., 8th (1991), Meeting Date 1990, 374-9. Editor(s): Tabuchi, Kazuo. Publisher: Springer,
Tokyo, Japan.
CODEN: 58CIAJ

L5 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN McCormick, Francis P.; Innis, Michael A.; Ringold, Gordon M.
TI Manufacture of glycosidated interferons with recombinant CHO cells
SO U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 438,911.
CODEN: USXXAM

L5 ANSWER 33 OF 47 MEDLINE DUPLICATE 20
AU Mercer W E; Shields M T; Amin M; Sauve G J; Appella E; Romano J W; Ullrich
S J
TI Negative growth regulation in a glioblastoma tumor **cell** line that conditionally **expresses human** wild-type p53.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Aug) 87 (16) 6166-70.
Journal code: PV3. ISSN: 0027-8424.

L5 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Caillet-Fauquet, P.; Perros, M.; Brandenburger, A.; Spegelaere, P.; Rommelaere, J.
TI Programmed killing of human cells by means of an inducible clone of parvoviral genes encoding nonstructural proteins
SO EMBO J. (1990), 9(9), 2989-95
CODEN: EMJODG; ISSN: 0261-4189

L5 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Johansen, Teit Eliot; Schoeller, Marianne Skak; Tolstoy, Susanne; Schwartz, Thue W.
TI Biosynthesis of peptide precursors and protease inhibitors using new constitutive and inducible eukaryotic expression vectors
SO FEBS Lett. (1990), 267(2), 289-94
CODEN: FEBLAL; ISSN: 0014-5793

L5 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Furuta, Yasuhide; Aizawa, Shinichi; Suda, Yoko; Ikawa, Yoji; Kishimoto, Hidehiro; Asano, Yoshihiro; Tada, Tomio; Hikikoshi, Atsuko; Yoshida, Mitsuaki; Seiki, Motoharu
TI Thymic atrophy characteristic in transgenic mice that harbor pX genes of human T-cell leukemia virus type I
SO J. Virol. (1989), 63(7), 3185-9
CODEN: JOVIAM; ISSN: 0022-538X

L5 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Brinkmann, A. O.; Faber, P. W.; Van Rooij, H. C. J.; Kuiper, G. G. J. M.; Ris, C.; Klaassen, P.; Van der Korput, J. A. G. M.; Voorhorst, M. M.; Van Laar, J. H.; et al.
TI The human androgen receptor: domain structure, genomic organization and regulation of expression
SO J. Steroid Biochem. (1989), 34(1-6), 307-10
CODEN: JSTBBK; ISSN: 0022-4731

L5 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Kramerova, I. A.; Zelenin, M. G.; Filyakina, N. S.; Kolobkov, S. L.

TI Cloned **human** erythropoietin gene **expression** in mammalian **cells** in vitro
SO Mol. Genet., Mik[redacted]biol. Virusol. (1989), (3), 43-[redacted]
CODEN: MGMVDU

L5 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Okano, Kiyoshi; Sawada, Ritsuko; Shimizu, Hirohiko
TI Interferons and their manufacture with recombinant animal cells
SO Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF

L5 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Okano, Kiyoshi; Sawada, Ritsuko; Shimizu, Hirohiko
TI Human lung cancer cells for manufacture of polypeptides
SO Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF

L5 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Okano, Kiyoshi; Sawada, Ritsuko; Shimizu, Hirohiko
TI Glycopeptides and their recombinant production with human cells
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF

L5 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Brunet, Lisa J.; Berk, Arnold J.
TI Concentration dependence of transcriptional transactivation in inducible E1A-containing human cells
SO Mol. Cell. Biol. (1988), 8(11), 4799-807
CODEN: MCEBD4; ISSN: 0270-7306

L5 ANSWER 43 OF 47 MEDLINE DUPLICATE 21
AU Zahm P; Hofschneider P H; Koshy R
TI The HBV X-ORF encodes a transactivator: a potential factor in viral hepatocarcinogenesis.
SO ONCOGENE, (1988 Aug) 3 (2) 169-77.
Journal code: ONC. ISSN: 0950-9232.

L5 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2000 ACS
IN Groner, Yoram Meonot Wolfson A.
TI Expression of superoxide dismutase in eukaryotic cells
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW

L5 ANSWER 45 OF 47 MEDLINE DUPLICATE 22
AU Magee A I; Gutierrez L; McKay I A; Marshall C J; Hall A
TI Dynamic fatty acylation of p21N-ras.
SO EMBO JOURNAL, (1987 Nov) 6 (11) 3353-7.
Journal code: EMB. ISSN: 0261-4189.

L5 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2000 ACS
AU Zettlmeissl, Gerd; Ragg, Hermann; Karges, Hermann E.
TI Expression of biologically active human antithrombin III in Chinese hamster ovary cells
SO Bio/Technology (1987), 5(7), 720-5
CODEN: BTCHDA; ISSN: 0733-222X

L5 ANSWER 47 OF 47 MEDLINE DUPLICATE 23
AU Klessig D F; Brough D E; Cleghon V
TI Introduction, stable integration, and controlled expression of a chimeric adenovirus gene whose product is toxic to the recipient human cell.
SO MOLECULAR AND CELLULAR BIOLOGY, (1984 Jul) 4 (7) 1354-62.
Journal code: NGY. ISSN: 0270-7306.

=> d bib 9 15

L5 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2000 ACS
AN 1997:265594 CAPLUS
DN 126:247559
TI Rodent whey acid protein (WAP) or **mouse mammary tumor virus (MMTV) regulatory sequences** for targeted **expression** of heterologous genes in **human** mammary **cells** and applications in carcinoma gene therapy
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
PA Bavarian Nordic Research Institute A/s, Den.; Gsf - Forschungszentrum Fuer Umwelt Und Gesundheit; Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9709440	A1	19970313	WO 1996-EP3922	19960906
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
	AU 9669876	A1	19970327	AU 1996-69876	19960906
	EP 848757	A1	19980624	EP 1996-931040	19960906
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11511979	T2	19991019	JP 1996-510876	19960906
PRAI	DK 1995-976	19950906			
	WO 1996-EP3922	19960906			

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L5 ANSWER 12 OF 47 MEDLINE DUPLICATE 7
AB The ability to respond to small signalling molecules such as steroid hormones is important for many physiological processes. Steroid hormones act through a group of high affinity receptors that regulate transcription by binding to hormone response elements (HREs) located within the promoters of target genes, which themselves are organized with nuclear proteins to form chromatin. To dissect the mechanisms(s) of steroid hormone action we have used the steroid inducible **mouse mammary tumor virus (MMTV) promoter** as a model system. The **MMTV promoter** is assembled into a phased array of nucleosomes that are specifically positioned in rodent cells. Induction of transcription by glucocorticoids is accompanied by the appearance of a hypersensitive region in the proximal promoter which allows the hormone dependent assembly of a preinitiation complex including transcription factors such as nuclear factor 1 (NF1) and the octamer transcription factor (OTF). Surprisingly, when introduced by transient transfection, the progesterone receptor (PR) is unable to activate this promoter in vivo, a finding that may result from its inability to alter **MMTV promoter** chromatin. In an attempt to investigate the failure of the PR to activate the **promoter**, we have stably introduced the **MMTV promoter** into **human** T47D breast cancer **cells**

that **express** high levels of the PR. In contrast to what has been observed previously in rodent cells, the MMTV templates resident in human breast cancer cells adopt a novel and constitutive open chromatin structure. The constitutively open chromatin structure is accompanied by the hormone independent loading of transcription factors including the PR and NF1. In T47D cells that stably express the glucocorticoid receptor, the **MMTV promoter** responds to glucocorticoids, but not progestins, and displays glucocorticoid induced restriction enzyme hypersensitivity and transcription factor loading. These findings suggest that the organization of the MMTV chromatin structure is dependent upon the cell type and receptor status of the recipient cell into which the **MMTV promoter** is stably introduced.

L5 ANSWER 13 OF 47 MEDLINE DUPLICATE 8

AB The regulatory element (RE) of the human leukosialin (LS)-encoding gene, that encodes a major sialoglycoprotein of human leukocyte and platelet membranes, was used to develop a novel expression vector, pKX. The vector was constructed by cloning a RE fragment and the SV40 fragment containing polyadenylation and splicing signals between HindIII and BamHI sites of the pCAT-Basic vector. The transcription level controlled by this vector was evaluated in six different cell lines using a transient expression assay of chloramphenicol acetyltransferase (CAT). The CAT activity of the pKX vector was compared to the other common expression vectors, namely pMSG (driven by the **mouse mammary tumor virus** LTR), pcDL-SR alpha (SV40 **promoter/enhancer** and HTLV-I LTR), pcDNAI (cytomegalovirus promoter/enhancer) and pCAT-Control (SV40 promoter/enhancer). The level of expression provided by the pKX vector was comparable to that observed with pcDNAI and pcDL-SR alpha vectors. In different mammalian cell lines, the highest efficiency of **expression** of the pKX vector was observed in the **human** T-**cell** lines, Jurkat and CEM, although the **expression** of pcDL-SR alpha-CAT in those cell lines was in the same range. The expression of the pKX vector driven by a non-viral promoter and/or enhancer can be as efficient as that driven by a viral promoter and/or enhancer. Potential uses of this vector may be found in studies of transient gene expression in hematopoietic cells and for gene therapy, particularly the ones involving T-cells.

L5 ANSWER 14 OF 47 MEDLINE DUPLICATE 9

AB Various combinations of promoters, introns and transcription terminators were used to drive the **expression** of bovine growth hormone (bGH) cDNA in different **cell** types. In constructs containing the **human** cytomegalovirus (hCMV) promoter and the SV40 late genes terminator, the intron from SV40 genes (VP1) was much more efficient, than the intron from the early genes (t). The synthetic intron SIS generated by the association of an adenovirus splice donor and an immunoglobulin G splice acceptor showed the highest activity. The respective potency of these introns was similar in several mammalian (CHO, HC11 and COS) and fish (TO2 and EPC) cells. The rabbit whey acidic protein (WAP) gene promoter was highly efficient to drive the expression of bGH gene in the HC11 mammary cell lines. In contrast, the bGH cDNA under the control of the same promoter was much less efficiently expressed when the SV40 VP1 intron and transcription terminator were used. The rabbit WAP gene and the human GH gene terminators did not or only moderately enhanced the expression of the construct WAP bGH cDNA. Introduction of a **promoter** sequence from the **mouse mammary tumor virus** (MMTV) LTR in the VP1 intron increased very significantly the expression of the WAP bGH cDNA. Although several of these vectors showed high potency when expressed stably in HC11 cells, all

of them were only moderately efficient in transgenic mice. These data indicate that the VP1 and the SIS introns may be used to express foreign cDNAs with good efficiency in different cell types. The addition of an enhancer within an intron may still reinforce its efficiency. However, transfection experiments, even when stable expression is carried out, are poorly predictive of the potential efficiency of a vector in transgenic animals.

L5 ANSWER 15 OF 47 MEDLINE DUPLICATE 10

AB PURPOSE. Human corneal endothelial cells are thought to have limited capacity for proliferation. Little is known about the mechanisms that regulate the proliferation of these cells. The authors introduced oncogenes into human corneal endothelial cells to modulate proliferation. In addition, they sought to establish cell lines to facilitate study of human corneal endothelial cells. METHODS. Early-passage human corneal endothelial cells were transduced with disabled retrovirus (pLXSN16E6/E7) coding for the human papilloma virus type 16 transforming oncoproteins E6 and E7. Early-passage cells were also stably transfected by electroporation with the pMTV-D305 plasmid vector, in which SV40 large T antigen (SV40 LTAg) mRNA expression is positively regulated by the **mouse mammary tumor virus promoter**. Expression of E6/E7 mRNA or SV40 LTAg mRNA in cell lines was monitored with the polymerase chain reaction. SV40 LTAg protein **expression** was detected by immunocytology and Western blot analysis. RESULTS. **Human** corneal endothelial **cells** were efficiently infected with disabled retrovirus coding for E6/E7, and seven strains of cells have continued active proliferation for more than 50 population doublings (PD) (< 8 control PD). E6/E7 mRNA was expressed by each cell strain. E6/E7 transformed cells proliferate rapidly and form a monolayer of cells with a high degree of contact inhibition. Transfection with pMTV-D305 is less efficient, and only a single strain was developed. pMTV-D305-transfected endothelial cells (dexamethasone induced) proliferated at a lower rate than E6/E7-transduced cells or cells transfected with a vector (pSV3neo) in which SV40 LTAg is constitutively regulated. In the absence of dexamethasone, the proliferation of pMTV-D305-transfected cells was even slower, but cells continued to produce SV40 LTAg mRNA and protein. The latter results indicated that SV40 LTAg mRNA continued to be synthesized at significant levels in pMTV-D305-transfected cells in the absence of the inducer dexamethasone. CONCLUSIONS. This study suggests that human corneal endothelial cells have a high capacity for proliferation. Thus, cell division is normally controlled in human corneal endothelial cells by poorly characterized, but efficient, mechanisms. Because the E6 and E7 proteins, as well as the SV40 large T antigen, specifically bind to and interfere with the activity of the retinoblastoma (RB) and p53 tumor suppressor proteins, our results suggest that these proteins have critical roles in regulating the proliferation of human corneal endothelial cells.

L5 ANSWER 16 OF 47 MEDLINE DUPLICATE 11

AB Transgenic mice were generated which express a truncated nuclear retinoic acid receptor beta (RAR beta), closely resembling the natural isoform RAR beta 4, under the control of the **MMTV promoter**. The transgene was expressed in salivary gland, testis, lung and mammary tissue in two different lines. At approximately 11-14 months virtually all the transgenic mice showed hyperplasia of the lung alveolar epithelium with an excess of type II pneumocytes. Hyperplasia of the mammary alveoli and terminal ducts was also seen in some females. Salivary glands and some sebaceous glands were hyperplastic in most male transgenic mice, but only

rarely in females or in non-transgenics. Primary benign and malignant tumours were more numerous in transgenic mice than in controls, with a total of 23 in 4[redacted]ice versus two in 33 non-trans[redacted]ic animals. Treatment with dexamethasone to increase transgene expression resulted in exaggerated versions of the above phenotypes. Overexpression of RAR beta 4 therefore appears to predispose various tissues to hyperplasia and neoplasia, and this by contrast to the RAR beta 2 isoform, which has tumour suppressor activity. A survey of ratios of RAR beta 4:RAR beta 2 **expression** in **human** lung tumour **cell** lines showed an increase compared with normal lung tissue, suggesting that RAR beta 4 may play a similar role in human tumorigenesis.

L5 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12

AB Previous studies suggest that secretion of cloned proteins synthesized by recombinant Chinese hamster ovary (CHO) cells can be ATP-limited. Other research indicates that the presence of cloned Vitreoscilla Hb (VHb) enhances ATP prodn. in O2-limited Escherichia coli. To evaluate the influence of VHb expression on recombinant CHO cell productivity, the vhb gene was fused to the **mouse mammary tumor virus** (**MMTV**) **promoter** and cloned in a CHO **cell** line previously engineered to **express human** tissue plasminogen activator (tPA). Western blot anal. confirms dexamethasone-inducible VHb expression in all of the clones tested. Batch cultivation expts. with a VHb-expressing clone and the parental CHO-tPA cells show a reduced sp. growth rate in the VHb-expressing cells. The VHb-expressing clone exhibits sp. tPA prodn. 40-100% greater than the parental CHO-tPA culture.

L5 ANSWER 18 OF 47 MEDLINE DUPLICATE 13

AB The T47D (A1-2) cell line is a **human** mammary carcinoma-derived **cell** line that has been engineered to constitutively **express** comparable levels of both glucocorticoid and progesterone receptors. In addition, these cells possess a stably integrated mouse mammary tumor virus (**MMTV**) luciferase reporter gene. Because the **MMTV promoter** is recognized similarly by both receptors, we have used this cell line to examine the transcriptional regulatory mechanisms employed by the two receptors. The stably integrated MMTV luciferase gene is highly inducible by glucocorticoids, whereas it is almost entirely refractory to induction by progestins. In contrast, a transiently transfected MMTV chloroamphenicol acetyl transferase reporter, while much more inducible by glucocorticoids, can be induced significantly by progestins. The differential inducibility of the stably integrated template is reflected in the superior ability of glucocorticoids to initiate alterations in the chromatin structure of the promoter. Concomitant with the changes in nuclease accessibility, glucocorticoids, unlike progestins, recruit transcription factors to the **MMTV promoter**. These results emphasize a central role for the modulation of the chromatin environment by steroid receptors in defining their capacity to regulate gene expression in vivo.

L5 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB Treatment of the MDA-MB-231 human breast carcinoma cell line with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) resulted in accumulation of the liganded Ah receptor complex in the nucleus, but no induction of the CYP1A1 gene was obsd. Transient transfection of MDA-MB-231 cells with the plasmid pRNH11c, contg. the intact human CYP1A1 regulatory region from -1142 to +2434 fused to the reporter gene, chloramphenicol acetyl transferase (CAT) showed no TCDD-induced CAT-expression, indicating that the lack of CYP1A1 induction is due to altered transcription factors

rather than mutated dioxin responsive elements (DRE's). MDA-MB-231 cells do not **express** a functional estrogen receptor (ER), a phenotype shared by other human breast cancer **cell** lines. To elucidate, whether a functional ER is required for Ah-responsiveness in MDA-MB-231 cells, a vector contg. the human ER cDNA, .DELTA.hER, was transfected into the cells. The basal CAT-activity did not change in the presence of the .DELTA.hER-plasmid. However, in cells treated with 10 nM TCDD, a significant increase in CAT-activity was obsd. Increasing the amt. of .DELTA.hER-plasmid transfected into the cells further increased CAT-activity. Transfecting the cells with the more simple construct, pMCAT 5.12, contg. one DRE in front of the **MMTV promoter**, mimicked the results obtained with pRNH11c, indicating that the restoration of TCDD-responsiveness by ER is mediated via the Ah receptor-DRE interaction. To test if the restoration of the function of the Ah receptor was due to overexpression of an unspecific nuclear factor, cells were transfected with a plasmid encoding the c-Jun protein. No TCDD-induced CAT expression was obsd. Cells cotransfected with plasmids encoding for c-Jun and ER resulted in decreased TCDD-induced CAT-activity compared to cells transfected with .DELTA.hER alone. Since c-Jun is known to downregulate the amt. of ER, the results support he hypothesis that the concn. of ER is a detg. factor in restoration of the function of the Ah receptor.

L5 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB The pathogenicity of the human c-erbB-2 oncogene was evaluated in transgenic mice. A DNA sequence comprising the **promoter-enhancer** region of the **MMTV** LTR and a constitutively activated allele of the human c-erbB-2 growth factor receptor gene was introduced into the germ line of mice. Expression of the transgene was obsd. in kidney, lung, mammary gland, salivary gland, Harderian gland, and in epithelial cells of the male reproductive tract. All transgenic mice expressing the c-erbB-2 receptor died within four months of birth. Histopathol. anal. suggests that preneoplastic lesions in kidney and lung most likely caused organ failure and the early death of the transgenic mice. Focal dilatation and atypical proliferation of the tubular epithelial cells was found in the kidney. These hyperplastic lesions were found adjacent to normal tubules. Immunohistochem. showed that normal renal structures were completely neg. for c-erbB-2 protein expression. Atypical pseudopapillary proliferation of bronchial and bronchiolar epithelial cells narrowed the bronchial lumen in lung. Alveoli appeared normal. The expression of c-erbB-2 protein was strictly limited to the proliferating epithelial cells and not detected in normal tissue. The mammary glands of two parous mice were underdeveloped, lacking lobular-alveolar structures and were lactation deficient. Only a few ducts were interspersed in the fat pad. A virgin mouse developed a focal adenocarcinoma infiltrating the mammary fat pad. Expression of the c-erbB-2 protein was enhanced in the proliferating epithelial cells. Transgenic males were sterile. Epithelial hyperplasia and hypertrophy in the epididymis, vas deferens and seminal vesicles was found. The transgene is not uniformly expressed in the tissues where the MMTV LTR is transcriptionally active. The scattered transgene expression invariably coincides with epithelial hyperplasia.

L5 ANSWER 21 OF 47 MEDLINE DUPLICATE 14

AB The parvovirus-encoded nonstructural (NS) proteins have been implicated in the cytopathogenicity of these agents. Although protein NS-1 of minute virus of mice (MVM) has been shown to be toxic, little is known about the role of NS-2 in this process. In order to determine the contribution of NS-1 and NS-2 to cytotoxicity, we took advantage of an expression system

controlled by the **mouse mammary tumor virus promoter** which responds to glucocorticoid stimulation and which controls the expression of both MVM(p) NS proteins. Different mutations were introduced in NS genes so as to affect the NS-1 or NS-2 protein. Neoplastic **human cell** lines **expressing** only NS-1 protein after induction by dexamethasone undergo a smaller lethality compared to lines expressing both wild-type proteins. Mutations that were introduced in NS-1 coding sequence and did not affect NS-2 were found to drastically suppress the cytotoxic effect. It is concluded that the NS-2 protein has little cytotoxic activity by itself but is required for the full **expression** of the viral cytopathic effect on transformed **human cells**. Furthermore these results lead us to suggest that the NS-2 cytotoxic domain is localized in the amino-terminal portion of the protein.

L5 ANSWER 22 OF 47 MEDLINE DUPLICATE 15

AB Prolactin plays a key role in the regulation and growth of mammary cells, and influences tumor promotion. We have shown that chronic energy restriction intake depresses prolactin levels, inhibits production of MMTV proviral DNA and proto-oncogene expression in mammary glands and prevents development of mammary tumors. Since the expression and proto-oncogene activation of **MMTV** are regulated by **promoter/enhancer** elements within its long terminal repeat (LTR), in the present study we used a chloramphenicol acetyl transferase (CAT) reporter gene system and gene transfection methods to study the effect of prolactin on MMTV LTR using a human ductal carcinoma cell line T47D stably or transiently transfected with a plasmid consisting of the LTR upstream of CAT gene. Human prolactin or dexamethasone induced, respectively, a 2-fold or 6-fold increase in CAT activity compared with background CAT activity in the absence of hormones. However, the combination of human prolactin and dexamethasone strongly enhanced (20-fold) induction of the LTR compared with the control. Human prolactin also showed a synergistic effect with progesterone on LTR induction. Both LTR and CAT genes needed to be linked for induction of CAT activity by prolactin and dexamethasone. Our results indicate that human prolactin can act synergistically with steroid hormones to regulate MMTV LTR-directed gene expression in transfected T47D cells.

L5 ANSWER 23 OF 47 MEDLINE DUPLICATE 16

AB The host's immune system discriminates tumor cells from normal cells by recognizing the major histocompatibility complex (MHC) class I antigen expressed on the tumor cell membrane. However, the role of MHC class I antigen in tumor cells has not yet been clarified. In this study, the influence of MHC class I antigen **expression** on the tumorigenicity of a **human** glioblastoma **cell** line (KMG4) is examined. Barely detectable levels of MHC class I messenger ribonucleic acid were found to express in KMG4 cells by Northern blot analysis using mouse MHC class I (H-2Ld) and human leukocyte antigen (HLA)-B7 genes as probes. The H-2Ld gene connected at the downstream end of **murine mammary tumor virus** (**MMTV**)-**promoter** was cotransfected with the neomycine-resistant gene pSV2-neo into KMG4 cells, and the drug-resistant cells were selected. The KMG4 cells (KMG4-MMTV-Ld), which acquired the MHC class I gene were detected by Northern blot analysis with H-2Ld as the probe, and by immunohistochemistry using the H-2Ld-specific monoclonal antibody. Tumorigenicity, as determined by colony-forming ability in soft agar, was then compared between MHC class I-expressing KMG4-MMTV-Ld and nonexpressing control cells. The MHC class I-expressing cells were found to be deprived of colony-forming ability, indicating that MHC class I antigen could negatively influence the anchorage-independent cell growth

of the human glioblastoma cell line KMG4.

L5 ANSWER 24 OF 47 MEDLINE DUPLICATE 17
AB Chimeric DNA expression vectors containing regulatory sequences proximal to the 5' end of coding sequences for mammalian genes provide valuable tools to study gene expression. Genes coding for easily measured products (reporter genes) can be used to study promoter strength and regulation of gene expression after transient expression of promoter-reporter constructs in mammalian cells. To determine the strength of a variety of mammalian and viral promoter-enhancer sequences in primary cultures of human mammary epithelial cells (HMEC), these sequences were fused to the bacterial chloramphenicol acetyltransferase (CAT) gene and transfected into HMEC using strontium phosphate. The long terminal repeat (LTR) of the endogenous murine leukemia virus AKR-623 was the most potent promoter of transient CAT expression in HMEC. A number of commonly available promoter sequences displayed a wide range of activities in these cells. The glucocorticoid responsive LTR **promoter** from the **murine mammary tumor virus** modulated expression of CAT and was sensitive to the concentration of dexamethasone in the growth media. In a similar fashion, the regulatory sequences from the murine metallothionein-1 gene retained responsiveness to zinc concentration in the growth media.

L5 ANSWER 25 OF 47 MEDLINE DUPLICATE 18
AB We have developed a simian virus 40 (SV40) T-antigen immortalized **human cell** line, 1MR90-D305.2H4 (IDH4), in which the **expression** of T-antigen is controlled by the **mouse mammary tumor virus** (**MMTV**) **promoter** and thus regulated by steroids such as dexamethasone. Studies on the regulation of proliferation by T-antigen led to the formulation of a two-stage model for human cell immortalization, in which a mortality stage 1 mechanism (M1) was the target of T-antigen action, and an independent mortality stage 2 mechanism (M2) produced crisis and prevented T-antigen from directly immortalizing cells. Rarely, a cell expressing T-antigen escaped crisis (e.g., M2) and was capable of indefinite proliferation. This model predicted that the deinduction of T-antigen in IDH4 cells would lead to the reexpression of the M1 mechanism, and thus a reexpression of the senescent phenotype. Our study confirms the prediction that, in the absence of steroids, IDH4 cells express a variety of morphological and biochemical markers characteristic of normal senescent human fibroblasts.

L5 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB The authors describe an investigation of mammalian expression systems for P450c21 (21-hydroxylase). Four different **promoters**, the SV40 early and late **promoters**, **MMTV**-LTR, and CMV immediate early **promoter** were tested for their ability to drive the expression of P450c21 in cultured COS-1 cells. With the exception of MMTV-LTR, all drove the expression of similar levels of functional 21-hydroxylase. In addn., the Rat-1 cell line was tested and shown to be suitable for the stable expression of functional P450c21. The authors have established cell lines derived from Rat-1 either normal or mutant P450c21 stably expressed together with amplifiable markers. The expression of P450c21 was further increased by selection in methotrexate.

L5 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB To facilitate the use of a wide range of selectable markers in transfection studies with **human cells**, in conjunction with the use of modulatable promoters for regulated **expression** of the genes of interest, two pUC19-based mammalian expression vectors, each contg. two lacZ.alpha.-based multiple cloning sites (MCS) were constructed. Selectable markers can be inserted into the MCS derived from

pUC19, and the recombinants can be screened by lacZ complementation. The genes of interest can be inserted into the second MCS. The new MCS contains an amber stop codon in-frame with translation of the LacZ .alpha.-peptide. The presence of insert in the second MCS can also be screened on XGal plates, but in an Escherichia coli host contg. an amber suppressor gene. Expression of the genes of interest can be modulated through transcription from the promoter of the mouse metallothionein-I-encoding gene or the long terminal repeat of the mouse mammary tumor virus. These vectors, as well as several of the intermediate plasmids described in this report, can be used to clone any two genetic elements into a single plasmid.

L5 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB Biol. active nerve growth factor .beta. (.beta.-NGF) suitable for pharmaceutical use is manufd. by expression of the cloned gene in animal cell culture. Expression in animal cell culture maximizes the yield of correctly folded protein. The coding region, starting from the codon for Met -121, was cloned by polymerase chain reaction amplification from placental DNA and put under the control of a metallothionein IIa promoter, or a simian virus 40 promoter enhancer and introduced into CHO-KI cells by std. methods.

L5 ANSWER 29 OF 47 MEDLINE DUPLICATE 19

AB A composite mammalian cell-E. coli shuttle vector was developed based on the human papova virus BK and pSV-neo. The vector contains a dioxin-responsive **enhancer** (DRE) controlling a **mouse mammary tumor virus** (**MMTV**) **promoter** for the inducible **expression** of inserted genes. In **human cells** the vector replicates episomally, presumably utilizing the BKV rather than the SV40 origin, and expresses the BK T/t antigens. A deletion in the late BK region precludes the expression of the core/capsid proteins VP1, VP2, and VP3, thereby preventing the infectious lytic cycle. HeLa cells which were transfected with this vector and selected for resistance to the antibiotic G418 maintained the construct primarily in episomal form during more than one year of continuous culture, with little or no integration into the host genome. Transformed cells cultured in higher concentrations of G418 contained higher copy numbers of the vector. This permits one to vary the dosage of an inserted gene easily and reversibly without the need of conventional amplification techniques and clonal analysis. Using a chloramphenicol acetyl transferase (CAT) reporter gene inserted downstream of the **MMTV promoter**, we found that CAT expression was greater in clones with higher vector copy number. CAT expression was inducible with 2,3,7,8-tetrachlorodibenzo-p-dioxin, but inducibility was found to be inversely proportional to the copy number. Transformation of bacteria with plasmid molecules retrieved from the mammalian host was efficient, making this vector well adapted for the screening of cDNA libraries for the ability to express a phenotype in mammalian cells. Moreover, DNA sequences were stable during long-term passage in mammalian cells; vector passaged continuously for more than one year retained fully functional bacterial genes for resistance to chloramphenicol and ampicillin.

L5 ANSWER 30 OF 47 SCISEARCH COPYRIGHT 2000 ISI (R)

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L5 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB The influence of MHC class I **expression** on **cell** growth was examd. in a **human** glioblastoma **cell** line (KMG4). Parental KMG4 cells expressing from low-to-undetectable levels of MHC class I mRNA were introduced with the mouse MHC class I (H-2Ld) gene with a **murine mammary tumor virus promoter**. Suppression of the colony-forming ability in soft agar was detected in MHC class I-expressing cells. Therefore, the expression of the MHC class I gene influences the anchorage-independent cell growth and suppresses the colony formation of a human glioblastoma cell line.

L5 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB Interferons with glycosidation patterns similar to those found in vivo are manufd. by expression of the cloned genes in CHO cells. Expression vectors using their own promoters or those from simian virus 40 (SV40) and mouse mammary tumor virus (MMTV) to drive expression of the cloned gene and a dihydrofolate reductase gene as selectable marker. The expression of the genes is superinducible using poly(I):poly(C) and cycloheximide. CHO cells transformed with plasmids expressing genes for interferons .alpha.76, .alpha.61, or .beta.1 from their own, or viral, promoters were superinduced as above. Genes expressed from the SV40 promoter showed no superinduction. Genes expressed from their own promoters showed superinduction of up to 100-fold with yields of interferon reaching 600,000 units/mL (60-fold induction). Anal. of patterns of glycosidation of the recombinant interferons showed that they were broadly similar to those of the naturally-occurring product.

L5 ANSWER 33 OF 47 MEDLINE DUPLICATE 20
AB To investigate the effect that human wild-type p53 (wt-p53) expression has on cell proliferation we constructed a recombinant plasmid, pM47, in which wt-p53 cDNA is under transcriptional control of the hormone-inducible **mouse mammary tumor virus promoter** linked to the dominant biochemical selection marker gene Eco gpt. The pM47 plasmid was introduced into T98G cells derived from a human glioblastoma multiforme tumor, and a stable clonal cell line, GM47.23, was derived that conditionally expressed wt-p53 following exposure to dexamethasone. We show that induction of wt-p53 expression in

exponentially growing cells inhibits cell cycle progression and that the inhibitory effect is reversible upon removal of the inducer or infection with simian virus 40. Moreover, when growth-arrested cells are stimulated to proliferate, induction of wt-p53 expression inhibits G0/G1 progression into S phase and the cells accumulate with a DNA content equivalent to cells arrested in the G0/G1 phase of the cell cycle. Taken together, these studies suggest that wt-p53 may play a negative role in growth regulation.

L5 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB Although its dependence on the target cell type is well established, the mechanism of cytopathogenicity of parvoviruses has remained elusive. Indirect evidence suggested that parvoviral non-structural (NS) proteins may be the cytotoxic effectors. In order to test this hypothesis, a mol. clone of parvovirus MVMp was modified, by replacing the P4 promoter of the NS transcription unit by the glucocorticoid-inducible **promoter** of the **mouse mammary tumor virus**. Clones of neoplastic human cells that had incorporated this construct and that were induced to produce NS proteins by dexamethasone, showed a cytopathic effect and eventually died. These data strongly suggest that the intracellular accumulation of parvoviral NS products jeopardizes the survival of the cells, which cannot be detected unless a threshold protein concn. is reached. A cell variant was isolated which resisted dexamethasone-induced killing, although it was fully inducible for the prodn. of NS proteins. This variant was also unusually resistant to infection with MVMp virions, thus confirming the essential role played by the NS proteins in the parvoviral cytotoxicity and indicating that the cytocidal activity of the parvoviral NS products is modulated by cellular factors that may vary from one cell to another.

L5 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB A series of expression vectors has been constructed based on the pML deriv. of pBR322. The eukaryotic transcription units employed various promoters followed by polycloning sites for 3-9 commonly used restriction enzymes and are completed by the SV40 polyadenylation sequence. In 4 of the vectors, designed for co-transfection or transient expression studies, only a single transcription unit contg. either a constitutive or an inducible promoter was incorporated. The human ubiquitin (UbC) promoter was used as a strong constitutive promoter, while the mouse metallothionein promoter and the promoter of the long terminal repeats of the **mouse mammary tumor virus** were used as inducible **promoters**. Another vector contained an addnl. transcription unit encoding a eukaryotic selection marker, the neomycin resistance encoding gene. The vectors were used in CHO cells and in neuroendocrine CA77 cells to synthesize peptide precursors, protease inhibitors and a protease. It is shown that these vectors are very efficient for the constitutive and inducible expression of nucleotide sequences in both transient and stable transfections of eukaryotic cells.

L5 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB The human T-cell leukemia viruses (HTLV) are assocd. with T-cell malignancies in humans. The malignant transformation occurs after a long latency in some carriers, and its mechanism appears to be distinct from that of other classes of retroviruses which induce transformation through viral or cellular oncogenes. A widely postulated explanation is that the products of novel pX genes transactivate endogenous cellular genes which lead to tumor development in T cells. To directly examine the pathol. effects of pX genes in vivo, transgenic mice were produced which harbored the HTLV type I pX gene under several different regulatory units: HTLV type I long terminal repeat, immunoglobulin **enhancer**-simian virus 40 **promoter**, and **mouse mammary**

tumor virus long terminal repeat. Atrophy of the thymus was characteristic in these mice regardless of the regulatory unit directing gene expression.

L5 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB A discussion and partial review with 22 refs. on the domain structure and the genomic organization of the human androgen receptor (hAR). The cDNA sequence reveals an open reading frame of 2751 nucleotides encoding a protein of 917 amino acids with a calcd. mol. wt. of 98,845. The N-terminal region of the hAR is characterized by a high content of acidic amino acid residues and by several homopolymeric amino acid stretches. The DNA-binding domain showed a high homol. with the DNA-binding domain of the human glucocorticoid receptor (hGR) and the human progesterone receptor (hPR). The predominantly hydrophobic steroid binding domain of the hAR is 50-55% homologous with the ligand binding domains of the hGR and hPR. Transient expression of recombinant AR cDNA in COS-cells resulted in the prodn. of a 110 kDa protein with the expected binding specificity of androgen receptors. Co-transfection with a reporter-gene construct [CAT (chloramphenicol acetyl transferase) under direction of the androgen regulated **MMTV-promoter**] showed that the protein is functionally active with respect to transcription regulation. In the LNCaP prostate carcinoma cell line 2 major (11 and 8 kb) and one minor (4.7 kb) mRNA species can be found which can be down-regulated by androgens. The hAR protein coding region was shown to be divided over 8 exons with an organization similar to that of the progesterone and estrogen receptor. The sequence encoding the N-terminal domain was found in one large exon. The 2 DNA-binding fingers were encoded by 2 small exons; the information for the androgen-binding domain was found to be distributed over 5 exons. Southern blot anal. of genomic DNA revealed that the hAR is encoded by a single gene, which is situated on the X-chromosome.

L5 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB The human gene coding for the principal factor of erythroid cell differentiation, erythropoietin, was isolated from a genomic phage library using an oligonucleotide probe. The construction of a series of plasmids carrying the erythropoietin gene under the control of various regulatory elements is reported. Efficiency of erythropoietin gene expression was estd. by testing the biol. activity of erythropoietin in conditioned media 45 h after transient transfection of COS1 and CHO cell lines.

L5 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB Expression vectors contg. eukaryotic promoters for expressing human interferons (I) are constructed for expressing in recombinant animal cells. Expression vector pMTV.beta. encoding I-.beta., contg. **mouse mammary tumor virus promoter** was constructed. Human lung cancer cell PC12 transformed with pMTV.beta. produced I-.beta. 100-4900 units/mL culture medium.

L5 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB Cell lines derived from human lung cancers are used for manufg. polypeptides such as interferons by expressing their genes from eukaryotic promoters. Expression vector pBPVMTV(Ha).beta. contg. **mouse mammary tumor virus promoter**, the whole genome of BamHI-digested BPV, and human interferon-.beta. (I-.beta.) gene was constructed. Human lung cancer cell line PC12 transformed with pBPVMTV(Ha).beta. produced I-.beta. 100-22300 units/mL culture medium.

L5 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB Vectors contg. eukaryotic promoters and bovine papilloma virus (BPV) DNA for **expressing** glycoproteins in **human cells** are constructed. [redacted]xpression vector pBPVMTV(Ha).b . contg. **mouse mammary tumor virus promoter**, the whole genome of BamHI-digested BPV, and human interferon-.beta. (I-.beta.) gene was constructed. Human lung cancer cell line PC12 transformed with pBPVMTV(Ha).beta. produced I-.beta. (100-20200 units/mL in the culture medium.

L5 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB The adenovirus E1A proteins are essential for the normal temporal activation of transcription from every other adenoviral early promoter. High-level E1A expression in the absence of viral infection would facilitate biochem. studies of E1A-mediated transactivation. Toward this end, the adenovirus type 2 E1A gene under the control of the **murine mammary tumor virus promoter** was introduced into HeLa cells. Uninduced cells expressed little or no detectable E1A mRNA. Upon induction, mRNA levels accumulated to about 50% of the level obsd. in 293 cells. The level of E1A expression in these cells could be controlled by varying the concn. of the inducing glucocorticoid. Under these conditions of varying E1A concns., it was obsd. that activation of the E2, E3, and E4 promoters of H5dl312 initiated at the same E1A concn. and that transcription from each promoter increased as the E1A concn. increased. Thus, E1A-mediated transactivation is proportional to the concn. of E1A protein. E1A-dependent transcriptional stimulation of the E4 promoter was reproduced in an in vitro transcription system, demonstrating that expression of only the E1A proteins was sufficient to increase the transcriptional activity of nuclear exts.

L5 ANSWER 43 OF 47 MEDLINE DUPLICATE 21

AB We report here on a transactivating function of HBV DNA. The effect is shown by stimulation of transient **expression** of pSV2cat DNA in cotransfected **human** liver CCL13 **cells**. Transfection experiments with plasmid constructs containing different HBV DNA fragments and Northern analyses of RNA from cells transfected with these recombinant plasmids indicate that a transactivating function is encoded within the X-ORF. A frameshift mutation within the X gene causes loss of activity thus demonstrating requirement of a protein. The increase in the level of CAT-specific RNA suggests that the transactivation is by transcriptional enhancement. Constitutive expression of the transactivator function was also observed in cells stably transfected with HBV DNA. A number of eukaryotic promoters, SV40-early, HSV-TK, HTLV-I and RSV LTRs were responsive to transactivation by HBV DNA. However, the **MMTV** LTR and the human metallothionein **promoter** (MTIIA) were considerably less responsive than the others. The transactivational potential of HBV DNA was much higher in human cells and cells of higher primates than in rodent cells, thereby indicating interacting cellular factors. These results introduce additional considerations for the role of HBV in the development of hepatocellular tumors.

L5 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2000 ACS

AB Plasmids are constructed contg. cDNA or gene encoding human Cu-Zn superoxide dismutase (SOD-1) for expression in eukaryotic cells (e.g. Hela, L) derived from multicellular organisms. Plasmid pmSV2-SOD-Neo and pSV-M.cSOD contain the SOD-1 cDNA under the control of the SV40 **promoter** and the **mouse mammary tumor virus promoter**, resp. Plasmid pHG-SOD-SV-Neo carries the cellular SOD-1 gene isolated from a human genetic library regulated by the SOD-1 native regulatory elements. Plasmid pmSV2-anti-SOD-gpt contains

the SV40 promoter and the SOD-1 cDNA, and further encodes an antisense SOD-1 mRNA which regulates the SOD-1 cDNA expression.

L5 ANSWER 45 OF 47 MEDLINE DUPLICATE 22
AB To study the acylation of p21N-ras with palmitic acid we have used **cells** which **express** the **human** N-ras gene to high levels under control of the steroid-inducible **MMTV**--LTR **promoter**. Addition of [3H]palmitate to these cells resulted in detectable incorporation of label into p21N-ras within 5 min, which continued linearly for 30-60 min. Inhibition of protein synthesis for up to 24 h before addition of [3H]palmitate had no effect on acylation of p21N-ras, suggesting that this can occur as a late post-translational event. Acylated p21N-ras with a high SDS--PAGE mobility is found only in the membrane fraction, whereas approximately 50% of the [35S]methionine-labelled p21N-ras is cytoplasmic and has a lower mobility.
Conversion of the acylated high mobility form to a deacylated form of slightly lower mobility can be achieved with neutral hydroxylamine, which is known to cleave thioesters. This treatment also results in partial removal of p21N-ras from the membranes. A remarkably high rate of turnover of the palmitate moiety can be demonstrated by pulse--chase studies (t1/2 approximately 20 min in serum-containing medium) which cannot be attributed to protein degradation. The data suggest an active acylation--deacylation cycle for p21N-ras, which may be involved in its proposed function as a signal transducing protein.

L5 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2000 ACS
AB Dihydrofolate reductase (DHFR) deficient chinese hamster ovary (CHO) cells were cotransfected with a plasmid contg. the human antithrombin III (AT III) cDNA preceded by the SV40 virus early promoter, and plasmids contg. the mouse DHFR cDNA under the control of either the **mouse mammary tumor virus** long terminal repeat (**MMTV**-LTR) **promoter** or without any known eukaryotic promoter. Cell clones were selected that expressed the DHFR-gene despite the absence of a promoter in the latter case. The AT III cDNA was efficiently expressed in both cell types. After amplification with methotrexate (MTX), various cell lines secreted up to 22 .mu.g AT III/106 cells/24 h. AT III was isolated from the medium of cultured cells and shown to be indistinguishable from human plasma derived AT III by immunol. criteria and biol. activity.

L5 ANSWER 47 OF 47 MEDLINE DUPLICATE 23
AB The DNA-binding protein (DBP) encoded by human adenoviruses is a multifunctional polypeptide which plays a central role in regulating the expression of the viral genes. To gain a better understanding of the relationships between the various functions provided by DBP, an extensive collection of DBP mutants is essential. To this end we have constructed several permissive **human cell** lines which contain and **express** the DBP gene at high levels to allow propagation of otherwise lethal, nonrecoverable mutants of DBP. Because DBP is toxic to human cells, cell lines were constructed by using a vector in which the DBP gene is under the control of the dexamethasone-inducible **promoter** of the **mouse mammary tumor virus**. The low basal levels of DBP synthesis in the absence of dexamethasone allows isolation and propagation of these cells. Addition of dexamethasone enhances DBP production 50- to 200-fold, and within 8 h its synthesis from the single integrated copy of the chimeric gene is 5 to 15% of that observed during peak DBP synthesis in infected human cells in which hundreds of copies of the DBP gene serve as templates. At the nonpermissive temperature, adenovirus mutants with ts lesions in the DBP

gene replicate their DNAs, express their late genes, and form infectious viral particles in these DBP+ cell lines but not in the parental HeLa cells.

=> d his

(FILE 'HOME' ENTERED AT 16:21:12 ON 14 NOV 2000)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:21:27 ON 14 NOV 2000

L1 10027 S (MURINE OR MOUSE)(W)MAMMARY(W)TUMOR(W)VIRUS OR MMTV
L2 2247 S L1(6A)(PROMOTER OR PROMOTOR OR REGULATORY(W)SEQUENCE OR ENHAN
L3 117802 S EXPRESS?(10A)(HUMAN(5A)CELL)
L4 100 S L2 AND L3
L5 47 DUP REM L4 (53 DUPLICATES REMOVED)
L6 1094 S WHEY(W)ACID(W)PROTEIN OR WAP
L7 252 S L6(6A)(PROMOTER OR PROMOTOR OR REGULATORY(W)SEQUENCE OR ENHA

=> s l3 and l7

L8 5 L3 AND L7

=> dup rem l8

PROCESSING COMPLETED FOR L8
L9 3 DUP REM L8 (2 DUPLICATES REMOVED)

=> d 1-3 au ti so l9

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AU Barash, Itamar; Faerman, Alexander; Richenstein, Moshe; Kari, Rachel; Damary, Golda-Meir; Shani, Moshe; Bissell, Mina J.
TI In vivo and in vitro expression of human serum albumin genomic sequences in mammary epithelial cells with .beta.-lactoglobulin and whey acidic protein promoters
SO Mol. Reprod. Dev. (1999), 52(3), 241-252
CODEN: MREDEE; ISSN: 1040-452X

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian
TI Rodent whey acid protein (**WAP**) or mouse mammary tumor virus (MMTV) **regulatory sequences** for targeted **expression** of heterologous genes in **human** mammary **cells** and applications in carcinoma gene therapy
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

L9 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G; Stinnakre M G; Pointu H; Puissant C; Houdebine L M
TI The effect of various introns and transcription terminators on the efficiency of expression vectors in various cultured cell lines and in the mammary gland of transgenic mice.
SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.
Journal code: AL6. ISSN: 0168-1656.